tion than is possible in the actual state of our knowledge of this body.

We hope to be able to carry out these further investigations, and to direct our attention to the optical activity of the coloured products of the decomposition of the hæmoglobin molecule, especially hæmochromogen and hæmatin and their coloured derivatives.

In conclusion, we have to express our thanks to the Managers of the Davy-Faraday Laboratory of the Royal Institution for the facilities which they afforded us in carrying on the optical part of our work.

'On the Nucleoproteids of the Pancreas, Thymus, and Suprarenal Gland, with especial Reference to their Optical Activity." By Arthur Gamgee, M.D., F.R.S., Emeritus Professor of Physiology in the Owens College, Victoria University, and Walter Jones, Ph.D., Associate Professor of Physiological Chemistry in the Johns Hopkins University. Received February 9,—Read February 12, 1903.

Part I.—Bibliographical and Critical.

In a research in which one of us was associated with Dr. A. Croft Hill, it was discovered that Hæmoglobin is a dextrorotatory body, whilst the interesting Histon-like albuminous substance Globin, which is obtained by the splitting up of Hæmoglobin under the influence of highly diluted hydrochloric acid, and of which the characters, no less than the mode of preparation, have only been known since the researches of Fr. N. Schulz, is a normally lævogyrous albuminous body.

These interesting observations naturally suggested the probability that the Nucleoproteids might, like Hæmoglobin, prove to be dextrogyrous, and the research of which the first results are contained in this paper is the outcome of this idea. The hypothesis has been fully confirmed, as will be shown in the sequel, and it has thus been proved that some of the members of a group of albuminous bodies of great importance in the life-history of the organism, are dextrorotatory bodies.

The preparation of nucleoproteids of such purity and especially so free from contaminating colouring matters as to yield solutions sufficiently transparent and colourless for polarimetric work, was a necessary preliminary to our special researches, and has led to the discovery of many facts of interest in relation to the chemistry of the nucleoproteids.

Preliminary Remarks concerning the "Nucleoproteids" and "Nucleins" and the Sense in which the Latter Term is used in the Present Paper.

By the term Nucleoproteids, we designate complex, or rather compound, albuminous substances which are the constituents of the nucleated protoplasm of all the organs of the animal body, but especially of the ductless, as well as of the secreting, glands. These bodies are characterised by the large quantity of phosphorus which they contain, by the constant presence of iron, and by the fact that under the influence of heat, by the action of acids, of alkalies, but especially of pepsin and hydrochloric acid, acting at temperatures favourable to their action, they split up into albuminous matters, and into so-called true (to distinguish them from pseudo-) nucleins. The latter differ from the mother nucleoproteids which yielded them, by the fact that they result from the splitting-off of a fraction of the albuminous molecules which these contained in their pristine and native condition. These secondary, or we may say, degraded nucleoproteids, "the nucleins," contain all the phosphorus originally present in the mother substance.

By the action of caustic alkalies and heat, the nucleins yield as products of decomposition, albuminous matters, and the so-called "nucleinic acids," bodies which vary in composition in the different nucleoproteids, but which are characterised by the fact that when heated with certain mineral acids, they yield as products of hydrolysis (Kossel), one or more of the purin-derivatives long known as "the xanthine bases," Adenin (Amidopurin), Guanin (Aminooxypurin), Hypoxanthin (Oxypurin), and Xanthin (Dioxypurin), as well as in many cases a base called Thymin, $C_5H_6N_2O_2$, a derivative of Pyrimidine.* At the same time, the phosphorus is separated as phosphoric acid.

Kossel, to whose fine researches we owe the greater part of our knowledge of the nucleinic acids, advanced the hypothesis (based on the great variation in the quantities of the xanthine bases which result from the hydrolysis of nucleinic acids of different origins) that there are four nucleinic acids, each of which yields one of the bases only. This theory of Kossel appeared to gain important support from Ivar Bang's† discovery of guanylic acid, a nucleinic acid obtained by the action of solution of potassium hydrate on the nucleoproteids of the pancreas, and which, as its name indicates, yields on hydrolysis one only of the purin-bases, viz., guanine. This hypothesis does not

* Walter Jones, 'Zeitschrift f. physiol. Chem.,' vol. 29 (1900), p. 26; H. Steudel u. A. Kossel, 'Zeit. f. physiol. Chem.,' vol. 29 (1900), p. 303; H. Steudel, 'Zeitschr. f. physiol. Chem.,' vol. 30 (1900), p. 539; vol. 39 (1901), p. 241.

† Ivar Bang, "Die Guanylsäure der Pancreasdrüse und deren Spaltungsprodukte," 'Zeitschr. f. physiol. Chem.,' vol. 36 (1898), p. 133.

appear to be in unison with the facts known to us (Schmiedeberg, Levene, W. Jones and G. H. Whipple, T. B. Osborne and I. F. Harris).*

Hammarsten,† to whose researches on the nucleoproteids and their relations to the nucleins we owe much of our knowledge of these bodies, would restrict the term "Nucleins" to the albuminous compounds of the nucleinic acids which remain undissolved after prolonged digestion with pepsin and hydrochloric acid. But this limitation appears to us undesirable and unphilosophical, and we think that the term nuclein, which it is convenient to retain, both for historical and descriptive reasons, should be applied to designate all those bodies resulting from the splitting-off of some, but only some, of the albuminous molecules originally forming part of the more complex nucleoproteid mother substance. It is in this sense that we shall in this paper employ the term nuclein, it being understood that every nuclein is to be considered a nucleoproteid, inasmuch as it is a compound of an albuminous body with a nucleinic acid or acids.

The Researches of Hammarsten on the Nucleoproteids of the Pancreas.

In his most interesting and suggestive paper published in the year 1894, Hammarsten gave an account of two nucleoproteids which he had obtained from the pancreas.

The first of these bodies he designated proteid-α. He ascertained that this body which, being soluble in water, is present in cold aqueous extracts of the pancreas, is precipitated by acetic acid, and that when boiled its solutions yield a coagulated albuminous substance, the substance remaining in solution being presumably nucleoproteid-β. Although Hammarsten fully recognised that the first or α-body was the mother substance, and that proteid-β was only a product of its decomposition, he devoted his attention to the latter, being actuated by the following reasons:—In the first place, his object being at that time to study the non-albuminous products of the pancreatic nucleoproteid, it appeared to him more simple and wiser to take as the starting-point of the investigation a material containing less albumin. The chief ground, however, for leaving the more interesting nucleoproteid provisionally uninvestigated was the great difficulty of obtain-

* O. Schmiedeberg, 'Archiv f. experiment. Path. u. Pharmak.,' vol. 43 (1899), p. 57; P. A. Levene, 'Zeitschr. f. physiol. Chem., vol. 32 (1901), p. 541; W. Jones and G. H. Whipple, 'Amer. Jour. of Phys.,' vol. 7 (1902), p. 423. See particularly the recent paper by Thomas B. Osborne and Isaac F. Harris, "Die Nucleinsäure des Weizenembryos," 'Zeitsch. f. physiol. Chem.,' vol. 36, Heft 2 (September, 1902), p. 85.

† Olof Hammarsten, "Zur Kenntniss der Nucleoproteïde," 'Zeitschr. f. physiol. Chem., vol. 19 (1894), p. 19.

ing it in any degree pure, attempts at purification being attended with such loss that the yield was too small.

Hammarsten remarked that among the impurities most difficult to separate was the blood-colouring matter, as well as another colouring matter which he believed to be produced by the action of the air on the nucleoproteid itself. Further, another impurity adhering to the nucleoproteid was found by Hammarsten to be trypsin, which he was unable to separate from it. He remarks, indeed, that the proteolytic activity of the substance is so intense that in no other way could he obtain so powerfully acting a trypsin.

Having, for the reasons above stated, abandoned the study of the interesting mother-substance, his nucleoproteid-α, Hammarsten then directed his attention to the β-body. This body, he did not seek to obtain by the decomposition of the mother substance, of which it is a product, but by adopting the following method:—he boiled the finely comminuted and perfectly fresh pancreatic gland of the ox in water and obtained, after filtration, a perfectly clear, faintly yellow solution, to which he added, after cooling, from 1 to 2 parts of hydrochloric acid, or from 5 to 10 parts of acetic acid per 1000 parts of the liquid. In this manner he obtained an abundant, white, flocculent precipitate. He dissolved the substance thus precipitated in water, with the aid of the least possible quantity of alkali and reprecipitated it by adding an excess of acid. By repeating this process several times, the body originally precipitated was purified, so far as such a method can effect the purpose.

It must be clearly insisted upon that, as Hammarsten himself pointed out, the so-called nucleoproteid-β does not represent an original proximate principle of the pancreas, but is a nuclein produced from the original mother nucleoproteid (or nucleoproteids ?) by the action of boiling water. It is certainly in no spirit of detraction or want of respect for the eminent Swedish chemist, that we add the remark that the study of a nuclein to be satisfactory should, if possible, take as its starting point the pure mother substance, of which it is a product of decomposition, rather than the animal tissue which contains that substance. In the case of Hammarsten's nucleoproteid-β, one can at present only assert that it is a nuclein or a mixture of nucleins produced by the action of boiling water on the nucleoproteids, properly so called, existing preformed in the tissue of the pancreas.

These strictures notwithstanding, we have to point out the remarkably interesting facts which were discovered by Hammarsten in the course of the investigation under review. He made a series of ultimate organic analyses of different specimens of this nuclein, and showed that whilst its solutions when boiled with Fehling's solution gave no trace of reduction, the body when heated on the water-bath with dilute sulphuric acid, furnished a highly reducing substance.

Although unable to separate the reducing substance in a state of purity, he succeeded in preparing an Osazone of constant melting point and the characters of which agree with those of the osazone of a pentose, an observation which absolutely coincides with the researches of Kossel and Bang, which establish the presence of a carbohydrate nucleus in the nucleinic acids and the formation of pentoses when they are subjected to the hydrolytic action of dilute mineral acids and heat. Further, Hammarsten showed that when his nuclein was decomposed by heating with a 3 per cent. solution of sulphuric acid on the water bath, a crystalline sediment often separated which, after being purified, was analysed and shown to consist of guanine sulphate. Later, at Hammarsten's instigation, Ivar Bang, continuing the investigation, prepared from Hammarsten's nuclein, the nucleinic acid to which he ascribed the name of Guanylic Acid.

Part 2.—Experimental.

On the Nucleoproteid of the Pancreas and on Certain Characters of the Nucleins which are associated with, or derived from, it.

A. *The Nucleoproteid.*

Method of Preparation.

The finely divided pancreas of the pig was treated successively with 50 per cent. alcohol, 75 per cent. alcohol, and 95 per cent. alcohol, and finally subjected to the action of absolute alcohol and ether, with the object of dehydrating it. The material thus obtained was extracted with successive portions of a 5 per cent. solution of ammonium acetate, the united extracts were filtered, and the perfectly clear fluid was poured into four times its volume of weak alcohol. The precipitate thus formed was washed by decantation with a large amount of dilute alcohol, and finally dried with absolute alcohol and ether. The object of this series of procedures was to remove the colouring matter of the gland, which is somewhat soluble in dilute alcohol, more so in an alcoholic solution of ammonium acetate, but soluble to a very slight extent in an aqueous solution of ammonium acetate. These manipulations also remove a large amount of inorganic salts, and render the coagulable albuminous substances insoluble.

A 2 per cent. aqueous solution of this raw material had only a pale yellow colour, and it was found that it could easily be examined in a tube measuring 220 mm. with the polarimeter, monochromatic sodium light being employed. The polarimeter was a "Halbschatten-Polarimeter" made by Schmidt and Haensch of Berlin. *The result of the examination was to show that the solution contained a dextrorotatory substance. The solution, moreover, failed to give any indication of the presence of a reducing substance, even by prolonged boiling with Fehling's solution*, and

was found to be rich in material which yields xanthine bases on hydrolysis with sulphuric acid.

The main portion of the gland substance, purified by the processes above described, was treated with 20 parts of water, and to the filtered solution acetic acid was added, drop by drop. When a quantity of acid had been added sufficient to bring the amount of acid in the entire solution to 1 per cent., a well-defined white, flocculent, precipitate separated. This precipitate of nucleoproteid was separated by the centrifuge, suspended in water, and treated with an extremely dilute solution of ammonia, drop by drop, and the reaction of the liquid continuously tested with litmus. A very small amount of alkali was needed to neutralise the adherent acetic acid, when the solution became neutral and remained so until approximately twice as much ammonia had been used as had been required to completely dissolve the nucleoproteid. Evidently, the nucleoproteid is, at least, a dibasic acid, whose acid ammonium salt is soluble in water and neutral to litmus.

Purification of the nucleoproteid was effected by alternate solution in ammonia and precipitation with a minimal quantity of acetic acid. The final solution was poured into five volumes of 95 per cent. alcohol, washed repeatedly by decantation with excessively large quantities of 95 per cent. alcohol and ether, and then placed in an exsiccator over sulphuric acid.

Optical Properties.

1. A weighed amount of the nucleoproteid was suspended in water and dissolved by the addition of a trace of ammonia. The solution was made up to a definite volume with water, and examined polarimetrically :

Weight of substance (W) ...	1·006 gramme.
Volume of solution (V)	25 c.c.
Observed angle (α).....	$+3^\circ\ 4'$
Length of tube (L).....	200 mm.

$$[\alpha]_D = +38^\circ{\cdot}1.$$

2. The results of the above observation were confirmed by the examination of another preparation of nucleoproteid.

Weight of substance	0·500 gramme.
Volume of solution.....	25 c.c.
Observed angle	$+1^\circ\ 30'$
Length of tube	200 mm.

$$[\alpha]_D = +37^\circ{\cdot}5.$$

The solution was treated with an excess of acetic acid and the precipitate filtered off. The filtrate was found to be inactive.

B. *Nuclein accompanying, and probably resulting from, the Nucleoproteid.*

Method of Preparation.

The aqueous extract of the purified gland substance to which acetic acid had been added until it contained 1 per cent. of the latter, and from which the nucleoproteid had thus been separated, was treated with 20 per cent. acetic acid added a drop at a time. When the liquid contained 2 per cent. of the acid not the slightest precipitation had occurred. Continued addition of acetic acid, however, soon caused a turbidity, and when the acidity reached 5—6 per cent., a well-defined flocculent precipitate fell. This precipitate, which we shall call nuclein, was separated by means of the centrifuge and, at a great cost of material, was twice washed with water, the washings being separated by centrifugalising. The washed nuclein was suspended in water, and solution of ammonia added cautiously, one drop at a time; when the nuclein was completely dissolved, the reaction of the liquid was still acid to litmus. This solution was poured into four volumes of 95 per cent. alcohol, and the precipitated nuclein washed and dried by the methods described in the case of the nucleoproteid.

The fluid from which the "nuclein" had been precipitated, as has been stated, was now poured into four volumes of alcohol, and the precipitate thus thrown down was washed and dehydrated by the action of alcohol and ether. This preparation, which is necessarily very impure and especially rich in organic salts, will be described and referred to as "residual material."

Thus, by fractional precipitation with acetic acid, in the presence of inorganic salts, we have obtained three preparations. The nucleoproteid, which is doubtless the body which Hammarsten denominated Proteid-α, is almost insoluble in pure water, but may be dissolved by minute quantities of ammonia and caustic soda. The body which we have termed nuclein, to indicate our opinion of its relation to the first substance, is soluble in water with the greatest ease.

By the addition of a trace of copper sulphate to a solution of the nucleoproteid in caustic soda a fine pink colour is produced, but not a shade of violet makes its appearance until a comparatively large amount of copper solution has been added, a reaction which resembles closely "the biuret reaction" with the proteoses. The "nuclein" by similar treatment gives only the faintest pink colour, the violet shade being observed even when a very small amount of copper sulphate is used, while the "residual material" produces a violet colour from the beginning.

It has recently been shown by one of us* that the nucleoproteid of

* Walter Jones and G. H. Whipple, "The Nucleoproteid of the Suprarenal Gland," 'Amer. Jour. of Phys.,' vol. 7 (1902), p. 423.

the pancreas, prepared in substantially the same manner as the preparations employed in the present research, yields, when subjected to hydrolytic treatment, two of the xanthine bases, viz., guanine and adenine, and in a ratio which closely approximates four equivalents of the former to one of the latter. The "nuclein" and "residual material" of the present research were also found to yield xanthine bases on hydrolysis with sulphuric acid. All the three preparations under discussion contain phosphorus, all are completely precipitated from aqueous or faintly alkaline solutions by the addition of a trace of hydrochloric acid, and all yield precipitates when their neutral solutions are boiled.

Optical Properties of the Nuclein.

We had convinced ourselves by the following experiment that the specific rotation of the substance which we have denominated "nuclein" would be found to be greater than that of the nucleoproteid, before we had the opportunity of making a careful optical examination of the former substance.

A perfectly neutral solution of the neucleoproteid was prepared by treating some of the substance with water and an insufficient amount of ammonia to effect complete solution. The filtered fluid, examined with the polarimeter in a 200 mm. tube, gave a rotation of 1° 46′. The solution was heated to boiling, and the coagulated albumin filtered off. The filtrate polarised in a 200 mm. tube gave a rotation of 1° 49′. Now, as is well known, the process of boiling, removing a portion of the albuminous matter previously forming part of the complex nucleoproteid molecule, converts the latter into a nuclein. As the length of the tube was the same, and the angle of rotation remained sensibly constant in our experiment, a decrease in the amount of matter in solution (equal to the coagulated albumin removed from it) must mean an increase in the specific rotation.

The following direct determination of the specific rotation of the nuclein was made. The body was dissolved in water, and as the fluid was somewhat coloured, it was examined in a shorter tube than those which we have usually employed :—

Weight of substance.....	1·009 gramme.
Volume of solution	50 c.c.
Observed angle.....	+1° 18′
Length of tube	100 mm.

$$[\alpha]_D = +64°{\cdot}4.$$

The solution was treated with hydrochloric acid to precipitate the nuclein, and the filtered fluid examined in a tube 200 mm. long. The rotation was slightly negative (0°9′). In reference to this observa-

tion, we have to remark that we noticed several times that very slight lævorotatory filtrates were obtained when hydrochloric acid was used for precipitating the proteid, and especially when the acid fluid was allowed to remain in contact with the precipitate. Presumably, the negative rotation is due to an optically negative acid albumin being formed, which is soluble in the dilute hydrochloric acid.

As in the case of the nucleoproteid, a solution of the nuclein yields a coagulum on heating, and the rotation of the solution is not appreciably changed. This would lead one to assume the existence of a nuclein of which the specific rotation is greater than $+64°{\cdot}4$. It can easily be proved that such a substance exists in the preparation which we have designated "residual material."

A weighed amount of this substance was dissolved in a measured volume of water. The solution was examined with the polarimeter, treated with hydrochloric acid, and the amount of matter determined in the filtrate, which was found to be optically inactive. The following data were obtained:—

Weight of substance taken	0·520 gramme.
Weight of optically inactive matter ...	0·269 ,,
Weight of optically active matter	0·251 ,,
Volume of solution	25 c.c.
Observed angle.....	+1° 38′
Length of tube.....	200 mm.

$$[\alpha]_D = +81°{\cdot}1.$$

C. Hammarsten's Preparation.

As we have already explained, Hammarsten's so-called nucleoproteid-β, which is obtained from an extract of pancreas made by boiling the finely comminuted gland in water must, *ipso facto*, be a nuclein. The results which we had obtained and which have been described, made it highly desirable that we should make an optical examination of this substance also. By slight departures* from the method described by Hammarsten, which were absolutely necessary to remove the colouring matter, but which cannot possibly have exercised any influence on the chemical nature of the product, we were able to prepare a nuclein which must have been identical with Hammarsten's preparation (nucleoproteid-β). The substance which we obtained is soluble in water, and gives a violet biuret reaction. Its solution was comparatively highly coloured, but possessed so great a rotatory

* We used ammonia for redissolving the nuclein, instead of a fixed alkali employed by Hammarsten. We also finally poured an aqueous solution of the nuclein into 95 per cent. alcohol, and washed by decantation with absolute alcohol and ether.

power that fairly satisfactory polarimetric observations could be made in solutions of great dilution. The substance is dextrorotatory. The following data were obtained :—

Weight of substance	0·200 gramme.
Volume of solution	25 c.c.
Observed angle (mean of eight readings) ...	0° 47′
Length of tube.....	100 mm.

$$[\alpha]_D = +97°{\cdot}9.$$

On the Nucleohiston of the Thymus Gland.

It would seem quite easy to obtain this substance in any desired quantity by following the very simple method which Lilienfeld described in twenty lines.*

This method leads, however, to a product whose solutions are highly opalescent, and an optical examination could not be thought of. The cloudiness is so persistent, that for a long time we were inclined to believe it to be a property inherent in the substance. We finally succeeded, however, in obtaining solutions almost as colourless and transparent as distilled water. It is only necessary to extract Lilienfeld's preparation with a 5 per cent. solution of ammonium acetate and filter. The fluid filters very slowly, but perfectly clear and continuously. The solution was poured into 95 per cent. alcohol, and the precipitated proteid washed and dried with alcohol and ether, as described in connection with other preparations mentioned in this paper. The substance thus obtained was submitted to polarimetric examination, the solution being made with the aid of very dilute ammonia. The following data were obtained :—

Weight of substance	2·023 gramme
Volume of solution	50 c.c.
Observed angle	+3° 20′
Length of tube.....	220 mm.

$$[\alpha]_D = +37°{\cdot}5.$$

On the Nucleoproteid of the Suprarenal Gland.

In a research carried on conjointly with G. H. Whipple,† one of us lately described the nucleoproteid of the suprarenal gland, and showed that this body is a thymo-nucleoproteid. Ultimate analyses showed that the nucleoproteids of the suprarenal gland of the ox and the

* Leon Lilienfeld, "Zur Chemie der Leucocyten," 'Zeit. f. physiol. Chem.,' vol. 18 (1894), p. 473.

† Walter Jones and G. H. Whipple, *op. cit.*, p. 423 (Sept. 1902).

sheep are identical, and scarcely differ in chemical composition from the nucleoproteid of the pancreas prepared substantially by the same method as that which has served for the researches described in this paper.

The following table exhibits the results of the ultimate analyses of these bodies, and, for purposes of comparison, the analyses made by Hammarsten of his preparation is also given:—

	Nucleoproteid of suprarenal gland of sheep.	Nucleoproteid of suprarenal gland of ox.	Nucleoproteid of pancreas of pig.	Hammarsten's preparation.
C	46·22	46·81	45·83	43·62
H	6·10	6·38	6·26	5·45
P	4·70	4·72	5·05	4·48
N	17·92	17·85	17·42	17·39

As closely as the analytical processes at command could determine, the nucleoproteids of the pancreas and the suprarenal gland yield guanine and adenine in the same relative proportions, and these appear to indicate that one molecule of a nucleinic acid, or of a nucleoproteid, may yield two different xanthine bases.

We must refer the reader to the paper quoted above for a description of a method of separating the nucleoproteid of the suprarenal gland. As is well known, the characteristic physiologically active constituent of this gland forms a dark brown pigment when exposed in aqueous solution to the oxidising action of the air. Aqueous extracts of the gland are therefore always highly coloured, and this colouring matter places great difficulties in the way of the preparation of substances from the gland which are intended for optical examination. While, therefore, the work on the nucleoproteid of the suprarenal gland is not as satisfactory as we could desire, it can nevertheless be stated most positively that this nucleoproteid also is dextrorotatory.

The method of isolation which we employed does not differ essentially from that employed in the research already referred to, except that the gland was extracted several times with acetic acid before removing the nucleoproteid. A substance was finally obtained which is too highly coloured for accurate polarimetric determinations, but which, even in the necessarily high dilutions which could alone be used, could easily be shown to be dextrorotatory.

The following data were obtained:—

Weight of substance	0·199 gramme.
Volume of solution	25 c.c.
Observed angle	+0° 23′
Length of tube	100 mm

$$[\alpha]_D = +48^{\circ}\cdot1.$$

The value of this rotation is liable to revision, but its direction is beyond question.

Before formulating the general conclusions which, it appears to us, may legitimately be deduced from the researches of which an account has been given in this paper, we may sum up our work in the following manner:—

Summary.

We have, in this paper, described six substances obtained from various glands and have given methods by which several of these may be isolated and obtained sufficiently free from colouring matters to admit of exact polarimetric determinations.

All six of these substances yield on hydrolysis, albuminous bodies, phosphoric acid, and purin derivatives, and all contain iron in stable combination; they are, therefore, all nucleoproteids in the wide sense of the term.

The methods of preparation were such as to exclude all dextrorotatory substances which are not of a proteid nature, and all preparations were shown to be free from substances which reduce Fehling's solution even on prolonged boiling. Nevertheless, all these substances were found to be dextrorotatory, having specific rotations for light of the wave-length of D which vary from 37°·58, that of the nucleohiston of the thymus gland, to 97°·9 that of Hammarsten's nuclein obtained from the pancreas and described by him as proteid.

General Conclusions.

1. The nucleoproteids (employing this term in its wider sense, as including the compounds of the nucleinic acids with albuminous substances) which are contained in the pancreas, the thymus, and the suprarenal gland are dextrorotatory albuminous compounds.

2. When a nucleoproteid, by the splitting-off of albuminous molecules, which in its original condition formed part of its more complex molecule, becomes converted into a nucleoproteid of the "nuclein" type, its specific rotation increases.

3. It is legitimate to infer that not only the well characterised and typical nucleoproteids which we have subjected to examination, but all the nucleoproteids, including in this term the so-called nucleins, form a class of dextrorotatory albuminous substances.

Whilst the facts which have come under our notice appeared to us so full of interest that it would not have been wise to defer their publication, we are perfectly alive to the importance of answering with the least possible delay a number of most interesting questions suggested by them. We are already actively engaged in the investigation of these questions and hope shortly to publish the results of our

enquiries. We trust, therefore, that during the next few months we may be permitted to work out so far as we are able, the problems which have been suggested by the new facts recorded in this paper.

Supplementary Bibliographical Note.

Since the above paper has been in print, it has come under the notice of one of us that the late Professor Alexander Schmidt, of Dorpat, in his published researches on the coagulation of the blood,* drew attention to the fact that among the soluble constituents of protoplasm was a body to which he gave the name of "Cytoglobin," and which he found to be dextrogyrous. So far as we are aware, this observation of A. Schmidt has never been noticed or quoted, either by systematic writers on physiological chemistry or by those who have devoted their attention to, or written upon, the subject which formed the life-work of the Dorpat professor. There can be no question that Schmidt's cytoglobin was an exceedingly impure mixture of nucleoproteids, an opinion which is based upon the fact that his substance contained 12·52 per cent. of ash, and that, on ultimate organic analysis, the amount of carbon found was 56·36 per cent., as compared with 45·83, the percentage of carbon in the nucleoproteid of the pancreas. Still the fact remains that this indefatigable worker, whose suggestive writings have been too little read, left data which prove that the so-called "Cytoglobin" was nucleoproteid in nature, though in no sense a definite proximate principle, and that this impure mixture of nucleoproteids was characteristically dextrogyrous.

March 4, 1903. A. G.

* Alexander Schmidt, 'Zur Blutlehre,' Leipzig, Verlag v. F. C. W. Vogel, 1892. Refer to the chapter entitled "Ueber den in Wasser löslichen Bestandtheil des Protoplasmas," &c. (pp. 127—142); 'Weitere Beitraege zur Blutlehre' (nach des Verfassers Tode herausgegeben). Wiesbaden, J. F. Bergmann, 1895. Refer to the chapter entitled "Zur Kenntniss des Protoplasmas und seiner Derivate" (pp. 201—249).